Tetrahedron 69 (2013) 9591–9599

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Substituent effect on the photochemistry of 4,4-dialkoxylated- and 4-hydroxylated cyclohexenones

Yu-Jen Chen [a], Hui-Ling Wang [b], Nelson R. Villarante [c], Gary Jing Chuang [a,*], Chun-Chen Liao [a,b,*]

[a] Department of Chemistry, Chung Yuan Christian University, Chung Li 32023, Taiwan
[b] Department of Chemistry, National Tsing Hua University, Hsinchu 30013, Taiwan
[c] Department of Physical Sciences and Mathematics, College of Arts and Sciences, University of Philippines, Manila, Philippines

ARTICLE INFO

Article history:
Received 19 August 2013
Received in revised form 10 September 2013
Accepted 12 September 2013
Available online 19 September 2013

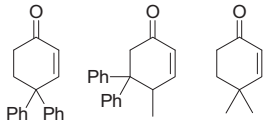
Keywords:
Photolysis
Cyclohexenone

ABSTRACT

Photochemistry of the title compounds in various solvents was studied using a broad band of light centered at 350 nm. C-4 spiroketal cyclohexenone **4** (1.0 M) afforded dimers and **12b** with the predominance of the former in polar solvent and the latter in nonpolar solvent. When the concentration was reduced to, **4** underwent solvent addition in nonpolar solvent and ring-contraction in polar solvents. 4,4-Dimethoxycyclohexenones **5a**–**d** in TFE exhibited a different photochemical behavior. The 5-vinyl-substituted enone afforded the bridged-bicyclic ketone **16**. Cyclohexenone **5b** with methyl moieties at C-2 and C-3 underwent aromatization whereas cyclohexenones with butyl substituent at C-5 and **5d** with silylated alcohol at C-2 underwent solvent exchange. In γ-hydroxylated cyclohexenones **6a**–**c** ring-contraction and solvent exchange were observed. Photochemistry of the title compounds from the mechanistic viewpoint is also described.

1. Introduction

The photochemistry of cyclohexenones has emerged as one of the most important topics of great interest both from the synthetic and mechanistic point of view. The cycloaddition reaction of cyclohexenones and its closely related monocyclic enones, the cyclopentenones, has been recognized as indispensable tool in the construction of carboxylic systems, which are intermediates in naturally occurring biologically active compounds.[1] The mechanistic interpretation of enone cycloaddition[2] and the molecular orbital interpretations on the electronics and reactivity of cyclohexenone rearrangements[3] have contributed so much in understanding the photochemical complexities of enone chemistry.



1 2 3

It is agreed upon through sensitization and quenching studies that most of the photochemical reactions exhibited by these systems, which involve deconjugation, reduction, solvent addition, dimerization, molecular rearrangement, and Diels–Alder reactions of cyclohexenones occur from the triplet excited state.[4] This diverse photochemical behavior of cyclohexenone systems is strongly controlled by the nature of substituents, media, and the low-lying triplet states. Dauben et al.[5] have conducted an extensive investigation on alkyl-substituted cyclohexenones and noticed that substitution at C-4 is critical for a lumiketone type of rearrangement; absence of these groups would lead to dimerization. Zimmerman, through a series of mechanistic explorations on cyclohexenones containing chromophoric moieties such as the diphenylcyclohexenone **1**[3e] has observed 1,2-migration of the aromatic moieties at C-4 whereas the diphenylcyclohexenone **2**[3f] afforded a four-membered carbocycle as the only product either under direct or sensitized irradiation. Chapman et al.[6] have observed lumirearrangement and ring-contraction of cyclohexenone **3** in *t*-BuOH during direct irradiation. Our lab has also studied the photochemical behavior of fused cyclohexenone system and found the preference of lumiketone rearrangement ($n \rightarrow \pi^*$) over hydrogen abstraction ($\pi \rightarrow \pi^*$) is governed by excitation mode during the photoreaction.[7]

Encouraged by these interesting findings on substituted cyclohexenones, we investigated the photochemistry of 4-dialkoxylated

* Corresponding authors. E-mail address: gjchuang@cycu.edu.tw (G.J. Chuang).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.09.037

cyclohexenones **4**, **5a**–**d**, and the 4-hydroxylated cyclohexenones **6a**,**b** and silyl protected **6c** (Fig. 1).

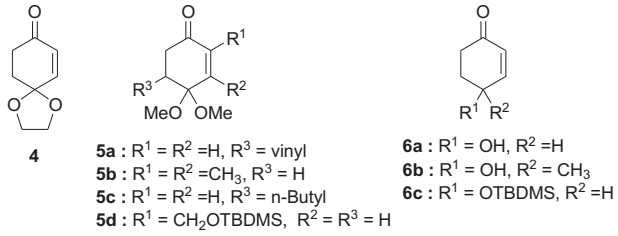


Fig. 1. Model systems for photochemical studies.

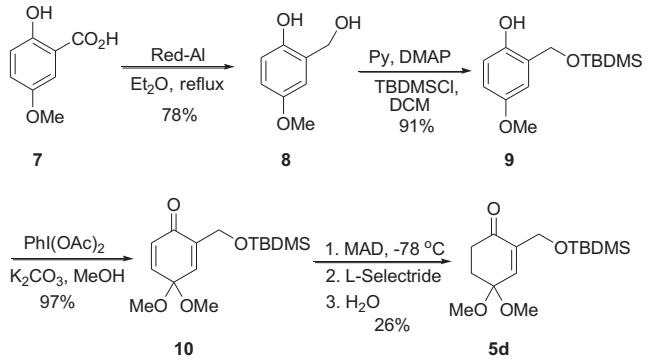
We envisaged that the presence of oxygen at C-4 might affect the reaction mode of cyclohexenones by influencing the intermediates of the reaction either through inductive or resonance effects. In addition, other structural moieties were introduced at the strategic positions of the alkoxylated cyclohexenones to evaluate its scope and limitation. Furthermore, solvents with varying degree of polarity were utilized in some reactions to evaluate solvent effect on product composition and distribution.

We herein report our interesting findings on the photochemical behavior of cyclohexenones **4**, **5**, and **6**.

2. Results

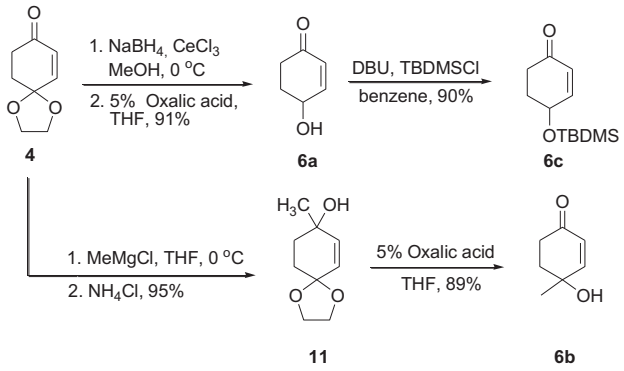
2.1. Synthesis of starting materials

Cyclohexenedione spiroketal **4** was used as our model system for the unsubstituted cyclohexenone as the synthesis of **4** was previously reported.[8] Another reason that we did not choose simple 4-dimethoxy cyclohexenone is its tendency of aromatization and exchange of the dialkoxy ketal in alcoholic solvent (as later shown in the photolysis of **5b**–**d**). Cyclohexenones **5a**–**c** were synthesized according to the procedures reported in the literature.[9] The dimethoxycyclohexenone **5d** was prepared in a four-step sequence starting from the reduction of 2-hydroxy-5-methoxybenzoic acid, **7** to produce the alcohol **8** in 78% yield (Scheme 1). Protection of the alcohol moiety with TBDMSCl under basic condition generated the silylated phenol **9** (91%), which upon oxidation with diacetoxyiodobenzene (DAIB) in methanol[8a] afforded the quinone monoketal **10** in excellent yield (97%). Selective conjugate reduction of the quinone was achieved using MAD[9] and L-selectride[10] as a carbonyl-complexing auxiliary to generate target photoenone **5d**.



Scheme 1. Synthesis of silylated cyclohexenone **5d**.

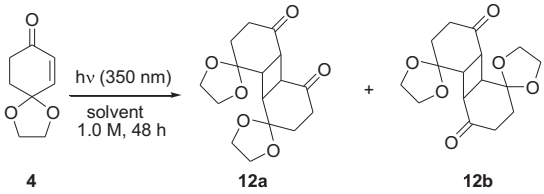
Cyclohexenones **6a**–**c** were prepared from cyclohexenone **4**. It began with the regioselective reduction of **4** using Luche reagent[11] followed by deprotection of the ketal with oxalic acid to generate the hydroxy ketone **6a** in 91% yield (Scheme 2). Upon addition of methylmagnesium chloride, **4** afforded spiroketal **11**; subsequent removal of the ethylene glycol protecting group with oxalic acid furnished cyclohexenone **6b**. Silylation of **6a** with TBDMSCl under basic condition afforded **6c**.



Scheme 2. Syntheses of cyclohexenones **6a**–**c**.

2.2. Photochemistry of cyclohexenedione spiroketal 4

A solution of cyclohexenone **4** (1.0 M) in benzene was bubbled with argon gas for 1 h and irradiated with a broad band of light centered at 350 nm in a Pyrex vessel in a Rayonet reactor for 48 h to afford the [2+2]-regioisomeric dimers **12a** and **12b** in 78% yield (Eq. 1). Gas chromatographic analysis of the mixed dimers in benzene, showed an HH (head-to-head, **12a**)/HT (head-to-tail, **12b**) ratio of 40:60 (Table 1, vide infra).



(1)

Table 1
Photochemical distribution ratios of dimers **12a** and **12b** in protic and aprotic solvents

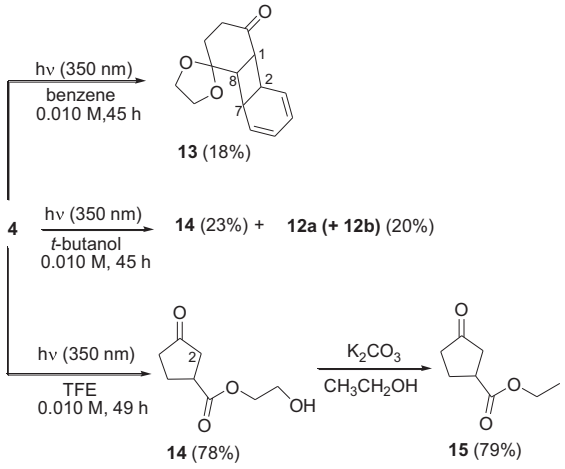
Entry	Solvent[a]	Dielectric constant (ε)	Ratio (**12a**/**12b**)[b]
1	Benzene	2.3	40:60
2	Ethyl acetate	6.0	53:47
3	*tert*-Butanol	10.9	55:45
4	Ethanol	25.0	67:33
5	TFE	26.5	69:31
6	Methanol	32.6	59:41
7	Acetonitrile	38.0	68:32

[a] Compound **4** (1.0 M) in different solvents was irradiated for 48 h in a Pyrex vessel with 350 nm light.
[b] Ratios were obtained from GC spectra by integrating the peak area. GC column: OV-17 1/8″×4 m detector, FID; flow rate, 18 mL/min; temperature gradient: 120–270 °C ramped at 10 °C/min.

Following the procedure we have at hand for the photo-transformation of **4** in benzene, we investigated the photochemical

behavior of this enone system in solvents of widely differing dielectric constants. As shown in Table 1, we noticed an apparent increase of **12a**/**12b** distribution ratio as the polarity of the solvent increases; however, a slight deviation from the trend was observed in the case of the methanol solvent.

At this point in the study, we decreased the concentration of **4** to 0.010 M using benzene, *tert*-butanol, and 2,2,2-trifluoroethanol (TFE) solvents and irradiated the resulting solution with 350 nm light. Irradiation of **4** in benzene for 45 h showed 82% conversion of the starting material, however, only the cycloadduct **13** (18%) generated by [2+2]-cycloaddition process could be characterized whereas in *tert*-butanol, a mixture of dimers **12a**,**b** (20%) and cyclopentenone **14** (23%) were produced (Scheme 3). Interestingly, irradiation of **4** in TFE for 49 h afforded **14** (78%) as the only isolable photoproduct, which can easily be trans-esterified with ethanol to furnish the keto-ester **15**[12] in good yield.



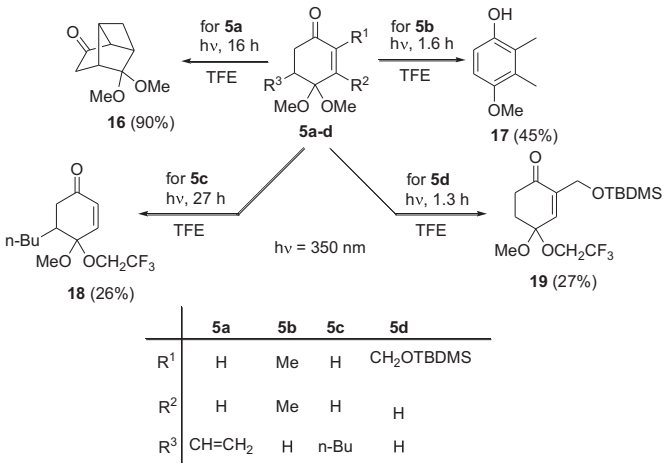
Scheme 3. Photochemical transformation of cyclohexenone **4** in solvents of varying polarities.

2.3. Photochemistry of 4,4-dimethoxycyclohexenones 5a–e

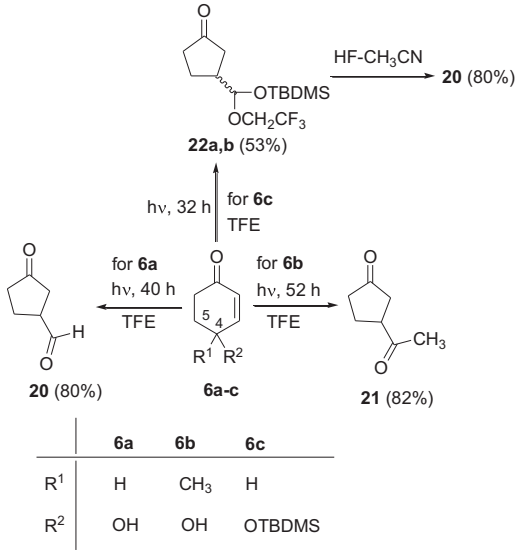
After fine-tuning the solvents, we selected TFE as solvent for the photochemical reactions of cyclohexenones **5a**–**d** because it gave both better yield and selectivity. Cyclohexenones **5a**–**d** in TFE were bubbled with argon for 1 h and irradiated with 350 nm light in a Pyrex vessel. Interestingly, cyclic enones **5a** and **5b** exhibited different photochemical transformations (Scheme 4); enone **5a** afforded the [2+2]-cycloadduct **16** in 90% yield after 16 h of irradiation whereas **5b** underwent aromatization producing **17** in considerable yield after 1.6 h of exposure to 350 nm light. No rearrangement products were observed for cyclohexenones **5c** and **5d** after irradiating for 27 h and 1.3 h, respectively; instead the cyclic ketones underwent solvent exchange generating the fluorinated cyclohexenones **18** and **19** in 26 and 27% yields, respectively.

2.4. Photochemical transformations of cyclohexenones 6a–c

Irradiation of cyclohexenone **6a** in TFE with 350 nm light for 32 h furnished cylopentanone **20** in 80% yield whereas illumination of 4-methylated cyclohexenone **6b** for 52 h afforded the diketone **21** in 82% yield (Scheme 5). Under the same reaction condition, the silylated cyclohexenone **6c** afforded stereoisomeric products **22a**,**b** with a combined yield of 53%. Desilylation of **22a**,**b** with HF–CH_3CN furnished a product whose spectral profile is similar to **20**.



Scheme 4. Photochemical transformations of cyclohexenones **5a**–**d**.



Scheme 5. Photochemical transformations of 4-hydroxy cyclohexenones **6a**–**c**.

3. Discussion

3.1. Structural elucidations of photoproducts

The gross structures of the two dimers were established as **12a** and **12b** based on spectral analyses and chemical correlations. High-resolution mass spectral analysis of the dimers showed a molecular ion peak (M^+) of 308. The dimers were differentiated based on their cyclobutyl spectral profiles. The HH stereochemical orientation of **12a** showed a α-tertiary carbon shift at δ 45.5, a little downfield than the HT orientation of **12b**, which showed an α-tertiary carbon shift at δ 44.2. This can be attributed to the proximity of the two electron-withdrawing carbonyl groups in **12a**, which deshield the cyclobutyl tertiary carbon. The major isomer **12b** showed its cyclobutyl tertiary protons as multiplet (m, 4H) with a chemical shift of 3.08 ppm whereas its stereoisomer **12a** exhibited two doublets for the same protons with a shift of 3.00 ppm (apparent d, J=7.1 Hz, 2H) and 3.23 ppm (apparent d, J=7.1 Hz, 2H); its coupling constant is indicative of a *cis*-vicinal hydrogen. The vicinal coupling constant shown for **12a** suggests that this dimer has *cis-anti-cis* configuration.

Structures **13** and **14** were established using spectral correlations. NOE spectra of **13** showed no interaction between C1–H and

C2–H; C7–H and C8–H, suggesting a *cis-anti-cis* configuration (see Supplementary data). The observed ^{1}H NMR shift of 3.86–4.07 ppm (m, 4H) and IR stretch of 1712 cm^{-1} for the glycol and carbonyl functional groups, respectively, were assigned to the spiroketal moiety of the cycloadduct. Elucidation of structure **13** was further substantiated by its proton chemical shift in $CDCl_3$, which showed a sharp doublet at δ 1.59 ppm (J=12.5 Hz) for the bridgehead C-8 proton; the large coupling constant is in agreement with the cis-relationship of C-1 and C-8 cyclobutyl protons. The two protons with δ values of 3.58 ppm and 3.77 ppm, respectively, and appeared as triplet can be attributed to the allylic protons of the cyclohexadiene moiety. For compound **14**, a saturated carbonyl IR stretch of 1728 cm^{-1} and hydroxyl stretch of 3410 cm^{-1} were observed along with ^{1}H NMR shifts of the diastereotopic protons at C-2 with δ values of 2.45 ppm (dd, J=18.1, 7.7 Hz, 1H) and 2.15 ppm (dd, J=18.1, 7.7 Hz, 1H). The hydroxyl IR stretch of **14** disappeared when it was trans-esterified with ethanol under basic condition, generating the keto-ester **15**, which showed the ethanolic ^{1}H NMR shifts of 1.16 ppm (t, J=7.2 Hz, 3H) and 4.05 ppm (q J=7.2 Hz, 2H). Compound **14** was further established using ^{1}H 2D-COSY (see Supplementary data).

For structure determination of **16**, an IR carbonyl absorption of 1727 cm^{-1} suggests a cyclic saturated ketone. No vinylic proton chemical shift was observed in the ^{1}H NMR; ^{13}C–^{1}H COSY spectrum is indicative of the tricyclic system of **16** (see Supplementary data). In the case of methoxyphenol **17**, we obtained a good spectral correlation with that reported in the literature.[13] Except for the proton chemical shift of the trifluoroethyl moiety, which was observed around 3.6 ppm, the spectral profiles of cyclohexenones **18** and **19** were similar to that of the starting materials.

^{1}H NMR, and ^{13}C NMR data for cyclopentenones **20** and **21** were in complete accord with the literature values.[14]

3.1.1. Solvent effects. The generality of [2+2]-cycloaddition reaction for cyclic enones, which occurs via triplet state is also observed in our model systems. Cyclohexenone **4** (1.0 M) in solvents of varying polarities generates dimers **12a**,**b** whose stereochemical orientations are observed to be *cis-anti-cis* HT (head-to-tail) and HH (head-to-head). Perusal on the data presented in Table 1, one can easily notice that photodimerization of **4** in nonpolar solvent such as benzene gives predominantly the HT dimer **12b** (**12a**/**12b**, 40:60) whereas in polar solvent such as ethanol, the regioselectivity is in favor of the HH dimer **12a** (**12a**/**12b**, 67:33). This kind of solvent effect is consistent with the photodimerization of α,β-unsaturated cyclohexenone and other cyclic enone systems.[15]

The effect of solvent on the dimer distribution ratios can easily be visualized by using the approach originally devised by Kirkwood and Onsager.[16] This analytical evaluation has been applied by de Mayo[17] to explain the dimerization of cyclopentenone systems. As shown in Fig. 2, a notable increase in **12a**/**12b** dimeric ratio is observed as the dielectric constant of the solvent increases. This result suggests that the transition state leading to the more polar dimer **12a** is stabilized by the polar solvent.[2b] Interestingly, the distribution ratios of the two dimers in methanol and *tert*-butanol are almost the same, however, the ε value of methanol is three times that of *tert*-butanol. Protonation of the enone excited triplet state with hydroxylic solvents may have influenced the distribution profiles of the products.[18] The observed change in **12a**/**12b** dimeric ratio with the polarity of the solvent suggests that the regioselectivity of the reaction can be effected by choosing an appropriate solvent. The distribution ratios of dimers **12a** and **12b** as a function of solvent polarity can be rationalized by either invoking Bauslaugh's[19] diradicaloid postulate or de Mayo's[20] dipole moment concept.

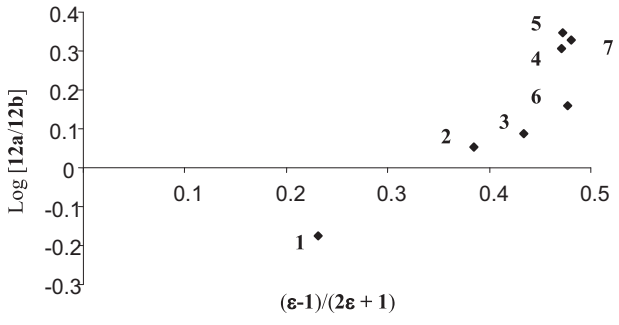
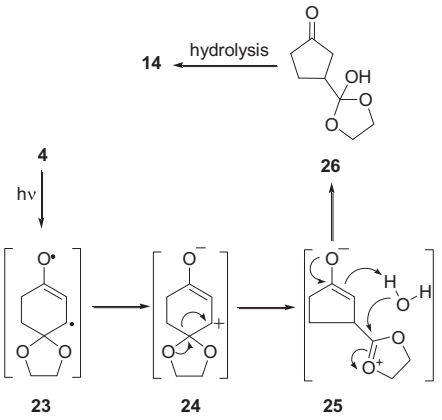


Fig. 2. Distribution ratios of dimers **12a** and **12b** as a function of dielectric constant (ε). Solvents: 1, benzene; 2, ethyl acetate; 3, *tert*-butanol; 4, ethanol; 5, 2,2,2-trifluoroethanol (TFE); 6, methanol; 7, acetonitrile.

Cycloaddition reaction of cyclohexenone **4** with a nonpolar solvent, benzene and the deep-seated photorearrangement of **4** in polar solvents such as *tert*-butanol and TFE were observed at very low concentration. The cyclic enone **4** behaved similarly, with the formation of **13** at very low concentration of enone, suggesting the dependency of photodimers on ketone **4** concentration. Apparently, dimerization process is less competitive at very dilute solution. In addition, the lone formation of cyclopentenone **14** in TFE solvent and the absence of this photoproduct in benzene solvent is indicative that solvation of intermediate in a polar medium is important for the formation of ring-contracted product such as **14**. As can be seen for slightly polar solvent (*tert*-butanol), both dimerization and ring-contraction processes were observed. This kind of perception is understood if we invoke a zwitterionic intermediate for the formation of **14**.

The mechanism of the reaction is thought to be as shown in Scheme 6, which involves excitation of the cyclic enone to a triplet state **24**, followed by electron demotion to generate **25**. Bond alteration gives intermediate **26**, which is subsequently attacked by adventitious water at the electrophilic site to furnish **27**; opening of the ketal moiety affords the keto-ester **14**. Ring-contraction to a five-membered ring and formation of zwitterionic intermediates as proposed here have ample precedent in the literature.[21,22] The [2+2]-cycloadduct **13** and the dimers **12a**,**b** may have been generated from the interaction of the excited triplet state **24** with the ground state benzene and cyclic enone **4**, respectively.[1a–i]



Scheme 6. Plausible mechanism for the phototransformation of cyclohexenone **4**.

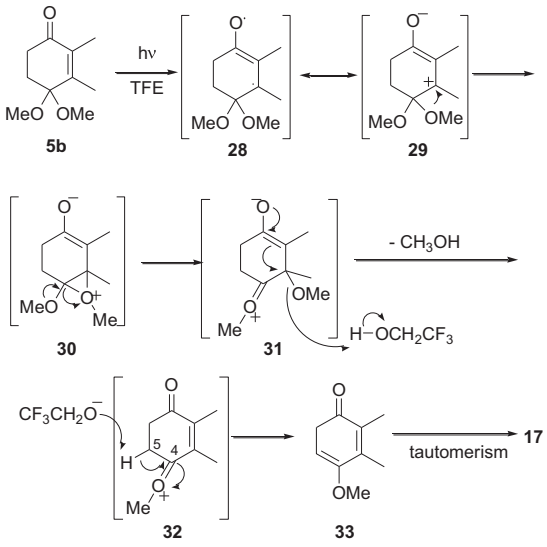
The [2+2]-cycloaddition reactions of cyclic α,β-unsaturated ketones to form cyclobutane derivatives have been successfully applied in many total syntheses of natural products and construction of highly strained molecules. The dimerization of cyclohexenone **4** and its cycloaddition with benzene to generate interesting photoproducts offer an excellent route to new four-membered ring systems, which can be elaborated further to

produce new materials of synthetic interest. The fused photoproducts are important precursors for the syntheses of highly-energetic benzene dimer, which can be a potential substrate in Diels–Alder reactions.[23]

3.2. Substituent effects and mechanistic considerations

The production of tricyclic ketone **16** from **5a** via intramolecular photocycloaddition reaction is an interesting photoproduct for this cyclohexenone system. Here we could see that although the breaking of C-4–C-5 bond in **5a** is facile, the proximity of the vinyl moiety to the enone system, which enforces orbital overlap and the inefficiency of vinyl group to undergo triplet excitation, which could have deactivated the molecule by twisting,[24] have enhanced the ease of [2+2]-cycloaddition process as manifested by the formation of **16** in excellent yield. Although there are other possible orientations for the interaction of the vinyl group with the enone, the resulting regioisomeric photoproduct is in accord with the Rule of Five.[25]

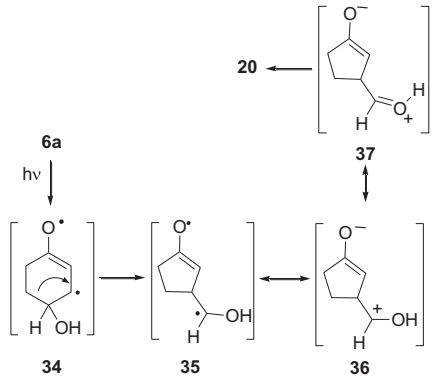
The presence of methyl substituents in **5b** has shifted the course of its photoreaction to a different direction, which involves the participation of the solvent during the photochemical event (Scheme 7). The mechanistic trail begins with intermediate **28**, followed by a charge-transfer mechanism to generate **29** and the oxonium intermediates, **30**–**32**. The final step involves hydrogen abstraction by the solvent to generate **33** followed by keto–enol tautomerism to furnish anisole **17**. Unlike cyclohexenones **5a**, the breaking of the C-4–C-5 bond in **5b** is less likely to occur because the incipient diradical formed during the cleavage process will be less stabilized by the unsubstituted C-5 carbon. In addition, the absence of the stabilizing substituent at C-5 and the presence of the methyl group at C-3 have enhanced the approach of the anionic solvent in abstracting the acidic hydrogen at C-5, thus aromatization occurred. This result is in contrast to that obtained by Dauben, et al.[5] for 2-methyl- and 3-methyl-substituted cyclohexenones wherein dimerization and deconjugation photoproducts were obtained.



Scheme 7. Plausible mechanism for the photorearrangement of **5b**.

Interestingly, phototransformation of cyclohexenone **5c** can also be accounted by employing the same mechanistic approach similar to that of **5b**, except that instead of abstracting hydrogen at C-5 like that in **32**, this is followed by nucleophilic attack of the solvent at C-4 to afford **18** (see Supplementary data). Although compound **5c** contains an abstractable hydrogen at C-5, the presence of the butyl group may have hindered the approach of the anionic solvent in abstracting the acidic hydrogen, consequently aromatization did not occur. Furthermore, the absence of other form of rearrangements such as lumirearrangement[5,6] indicates that the ability of the butyl substituent to stabilize an incipient radical or carbonium ion intermediate is insufficient to cause rearrangement. In the case of cyclohexenone **5d**, the mechanistic trail for the formation of **19** is thought to be similar to that of **5c**. The postulated zwitterionic intermediates for cyclohexenones **5a**–**d** are strongly supported by the formation of photoproducts **18** and **19** where the presumed cations are trapped by the solvent.

In the case of the 4-hydroxylated cyclohexenones **6a**–**c**, a careful scrutiny of the photoproducts also suggests a zwitterionic intermediates as evidenced by the constellation of the solvent in photoproducts **22a**,**b**. A plausible mechanism for **6a** is presented in Scheme 8. Irradiation of **6a** gives diradicaloid intermediate **34** through a bond-switching reaction to form the five-membered ring intermediate **35**. Electron demotion leads to the formation of the zwitterionic intermediates **36** and **37**. Rearrangement of the enolate affords the photoproduct **20**.



Scheme 8. Plausible mechanism for the phototransformation of cyclohexenone **6a**.

The observed photochemical behavior of cyclohexenones **6a**–**c** is interesting since 4-alkyl-substituted cyclohexenones usually undergo dimerization and 1,3-hydrogen rearrangement;[5] however, for 4-dialkyl-substituted cyclohexenones lumirearrangement along with other side photoproducts are usually observed.[3,4b] In the study conducted by Chapman et al.[6] on the photochemical rearrangement of 4,4-dimethylcyclohexen-2-one in acetic acid, various rearrangements along with substitution and elimination products were obtained implying a very low regioselectivity. In our model system the constellation of the hydroxyl group at C-4 enhances the selectivity of cyclohexenone rearrangement. The ring-contraction of 4-hydroxylated cyclohexenones will be advantageous from the synthetic viewpoint because this process generates a carbonyl moiety, which can easily be elaborated to construct potentially viable molecular frameworks for target-directed synthesis.

4. Conclusion

We have successfully unraveled interesting photochemical properties of cyclohexenones **4** and **5a**–**d** and the γ-hydroxylated cyclohexenones **6a**–**c**. The apparent change in dimeric ratios of the photoproducts of **4** in solvents of different polarities and the variation in photoproduct compositions of cyclohexenones **5a**–**d** and **6a**–**c** suggest that for target-directed synthesis, the influence of solvent, concentration, and substituent on the stereochemical

outcome of the reaction should be a priori to obtain the desired product with high degree of regio- and stereoselectivity. The interesting photoproducts of **4** can be potential substrates for constructing the elusive benzene dimers, which can be utilized in Diels–Alder reaction to generate new materials. The intramolecular [2+2]-cycloaddition reaction of **5c** will find its way in the construction of bridged-bicyclic systems, an important molecular framework for constructing natural product building blocks. γ-Hydroxylated cyclohexenones, **6a–c** unlike their analogues, the 4-alkylated cyclohexenones, generate products with high degree of selectivity; the photoproducts, which contain functionalized five-membered rings make them attractive for synthetic applications.

From the mechanistic viewpoint, the triplet excited state of cyclic enones, which is presumably involved in the photochemical event, is obviously affected by the polarity of the solvent as exemplified in the dimerization of **5**; an increase in HH/HT dimeric ratio as a function of the solvent dielectric constant indicates the polar nature of the HH transition state over that of the HT. In cyclohexenones **5a–d** and γ-hydroxylated cyclohexenones **6a–c**, the participation of polar protic solvents such as water and trifluoroethanol during the photochemical process is indicative of a zwitterionic intermediate.

5. Experimental section

5.1. 4-Hydroxy-3-(hydroxymethyl)anisole (8)

A solution of 2-hydroxy-5-methoxybenzoic acid (**7**) (849.5 mg, 5.0 mmol) in ether (5 mL) was placed in a reaction flask and added slowly with Red-Al (6.0 mmol) while being heated at reflux for 40 min. After the reaction was complete, the mixture was quenched by adding water (2 mL) and HCl (1.0 M, 2 mL). The mixture was extracted with ethyl acetate (20 mL×5) and the combined organic layer was collected, washed with saturated NaCl, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified in a silica gel column (hexanes/ethyl acetate, 1.5:1) and then recrystallized from dichloromethane to afford a white solid **8** (610.0 mg, 78%) (mp 75–76 °C). The ^{1}H NMR is in complete accord with the literature values.[26] IR (KBr plate) 3440, 3185, 1513, 1443, 1219, 1164, 1039, 1001, 864, 818, 759, 702 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 149.6, 125.7, 117.0, 114.3, 113.6, 64.2, 55.8; MS (EI, 75 eV) *m*/*z* (rel intensity) 154 (M^+, 32), 152 (2), 136 (100), 121 (4), 110 (5), 108 (45), 93 (7), 78 (25), 65 (29), 53 (8); HRMS (EI) calcd for $C_8H_{10}O_3$ 154.0630, found 154.0636. Anal. Calcd for $C_8H_{10}O_3$: C, 62.33%; H, 6.54%. Found: C, 62.19%; H, 6.61%.

5.2. 4-Hydroxy-3-(*tert*-butyldimethylsiloxymethyl)anisole (9)

A mixture of anisole **8** (153.0 mg, 1.0 mmol) and *N*,*N*-4-dimethylaminopyridine (DMAP) was vacuum dried under N_2 and added with dichloromethane (DCM) (5.0 mL), pyridine (0.5 mL), and TBDMSCl (1.0 M in CH_2Cl_2, 4.0 mL) at room temperature. The reaction mixture was stirred for 4 h and then quenched with HCl (0.10 M, 12 mL×2) and extracted with DCM (20 mL×2). The combined organic layer was stripped off of solvent and the residue was purified by flush column chromatography (hexanes/ethyl acetate, 15:1) to furnish a colorless oily liquid **9** (242.7 mg, 91%). IR (neat) 3388, 2943, 2858, 1502, 1465, 1250, 1154, 1052, 839, 780 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (br s, 1H), 6.78 (d, *J*=8.8 Hz, 1H), 6.71 (dd, *J*=8.8, 2.9 Hz, 1H), 6.55 (d, *J*=2.9 Hz, 1H), 4.84 (s, 2H), 3.72 (s, 3H), 0.92 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 150.0, 125.0, 116.9, 113.6, 112.3, 65.4, 55.6, 25.6, 16.0, −5.6; MS (EI, 75 eV) *m*/*z* (rel intensity) 268 (M^+, 18), 253 (0.5), 223 (0.1), 211 (100), 195 (6), 193 (13), 136 (20), 108 (1), 75 (0.5); HRMS *m*/*z* (M^+) calcd for $C_{14}H_{24}O_3Si$ 268.1495, found 268.1495.

5.3. 4,4-Dimethoxy-2-(*tert*-butyldimethylsiloxymethyl)cyclohexa-2,5-dien-1-one (10)

Anisole **9** (353.0 mg, 1.32 mmol) was mixed with K_2CO_3 (200.6 mg, 1.45 mmol), vacuum dried under N_2, and added with MeOH (13.2 mL). The solution was cooled to 0 °C and gradually added with $PhI(OAc)_2$ (1.0 M in MeOH, 14.5 mL) until the red-orange color became permanent, after which the solution was stirred for 10 min and then quenched with water (14 mL). The solvent was removed under reduced pressure and the residue was extracted with ether (20 mL×3); the organic layer was collected, washed with saturated NaCl, dried (Na_2SO_4), filtered, and concentrated to afford a yellowish oily liquid, **10** (380.9 mg, 97%). IR (neat) 2914, 1662, 1465, 1408, 1250, 1092, 964, 845, 779, 667 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 7.19 (dd, *J*=3.2, 2.2 Hz, 1H), 6.51 (dd, *J*=10.4, 3.2 Hz, 1H), 6.15 (d, *J*=10.4 Hz, 1H), 4.68 (d, *J*=2.2 Hz, 2H), 3.19 (s, 6H), 1.04 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 185.4, 144.2, 140.1, 137.4, 130.3, 94.0, 60.5, 50.4, 26.6, 19.1, −5.8; MS (EI, 75 eV) *m*/*z* (rel intensity) 297 (M^+−1, 0.02), 267 (3), 241 (100), 226 (2), 211 (89), 196 (11), 181 (6), 167 (1), 136 (2), 89 (1), 75 (4); HRMS *m*/*z* (M^+) calcd for $C_{15}H_{26}O_4Si$ 298.1601, found 298.1575.

5.4. 4,4-Dimethoxy-2,3-dimethyl-2-cyclohexenone (5b)

In a reaction flask, 2,6-di-*tert*-butyl-4-methylphenol (BHT) (720.0 mg, 3.30 mmol) was introduced and vacuum dried under N_2. Toluene (16.4 mL) was added at room temperature and the mixture was stirred to dissolve the solid. The reaction mixture was added with trimethylaluminum (2.0 M in hexane, 0.82 mL, 1.64 mmol) and stirred (30 min) until no more methane gas was detected. The solution was cooled to −78 °C and added with 2,3-dimethyl-4,4-dimethoxycyclohexa-2,5-dienone (380.9 mg, 1.28 mmol) in toluene (0.82 mL); a purple-black color was observed. L-Selectride (1.0 M in Et_2O, 0.98 mL) was gradually added until the solution turned light-yellow, after which saturated $NaHCO_3$ (1 mL) was added to quench the reaction. The mixture was brought to 0 °C, stirred for 30 min, filtered using Celite, and concentrated under reduced pressure. The residue was purified by flush column chromatography (hexanes/ethyl acetate, 100:1) to afford a colorless liquid **5b** (240 mg, 62%). IR (neat): 2957, 1672, 1443, 1377, 1316, 1215, 1142, 1078, 1051, 889 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 3.04 (s, 6 H), 2.59 (t, *J*=6.6 Hz, 2H), 1.89 (s, 3H), 1.88 (s, 3H), 1.86 (t, *J*=6.6 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 196.7, 152.4, 134.8, 98.4, 49.5, 34.7, 31.3, 16.3, 12.0; MS (EI, 75 eV) *m*/*z* (rel intensity) 184 (M^+, 4), 169 (3), 153 (70), 141 (18), 137 (15), 125 (100), 113 (5), 109 (2), 43 (24), 101 (12), 81 (1); HRMS (EI) calcd for $C_{10}H_{16}O_3$ 184.l099, found 184.1102.

5.5. 4,4-Dimethoxy-2-(*tert*-butyldimethylsiloxymethyl)-2-cyclohexenone (5d)

Following a similar procedure described for **5b**, a solution of **10** (380.9 mg, 1.28 mmol) in toluene furnished a yellowish liquid **5d** (100.8 mg, 26%). IR (neat) 2939, 1682, 1464, 1254, 1115, 1055, 1005, 928, 843, 777 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 7.19 (br s, 1H), 4.65 (d, *J*=2.4 Hz, 2H), 3.14 (s, 6H), 2.53 (t, *J*=6.4 Hz, 2H), 1.90 (t, *J*=6.4 Hz, 2H), 1.04 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 196.9, 140.4, 139.3, 96.8, 59.6, 47.9, 34.7, 31.3, 25.5, 18.0, −5.9; MS (EI, 75 eV) *m*/*z* (rel intensity) 300 (M^+, 2), 253 (2), 243 (100), 211 (56), 183 (5), 169 (20), 155 (8), 136 (1), 123 (1), 109 (7); HRMS *m*/*z* (M^+) calcd for $C_{15}H_{28}O_4Si$ 300.1757, found 300.1746.

5.6. 4-Hydroxy-2-cyclohexen-1-one (6a)

A solution of **4**[8a] (3.03 g, 19.67 mmol) in MeOH (49 mL) was added with $CeCl_3\cdot 7H_2O$ (7.33 g, 19.69 mmol) and stirred at 0 °C for 30 min while gradually adding $NaBH_4$ (0.37 g, 9.80 mmol). The

reaction mixture was quenched with ice-water and stirred for another 5 min before adding 5% oxalic acid (20 mL). Stirring was continued for another 30 min and then $NaHCO_3$ was added to adjust the pH to 6–7 before extracting the mixture with ether/ethyl acetate solvent system. After solvent workup, the residue was purified in a silica gel column (hexanes/ethyl acetate, 2:3) to provide a colorless liquid **6a**[27] (2.01 g, 91%).

5.7. 4-Hydroxy-4-methyl-2-cyclohexen-1-one (6b)

Cyclohexenone **4** (554.7 mg, 3.60 mmol) was placed in a round-bottom flask and vacuum dried under N_2. Dried THF (3.2 mL) was added under ice-bath and the resulting mixture was added with MeMgCl (20% in THF, 1.61 mL, 4.32 mmol). The reaction mixture was stirred at room temperature for 12 h before adding saturated NH_4Cl to quench the excess MeMgCl and then extracted with ether (3×). After solvent work up, a crystalline solid of **11** (583.2 mg, 95%) was obtained. IR (neat) 3382, 2951, 1664, 1388, 1207, 1090, 1035, 927 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 5.83 (d, J=10.1 Hz, 1H), 5.65 (d, J=10.1 Hz, 1H), 3.67–3.59 (m, 4H), 2.83 (s, 1H), 2.17–1.87 (m, 4H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.0, 128.0, 105.6, 67.3, 64.4, 36.3, 31.5, 28.2; MS (EI, 75 eV) m/z (rel intensity) 170 (M^++4), 155 (9), 152 (9), 142 (46), 112 (100), 99 (52), 91 (9), 83 (20), 63 (22), 45 (30), 33 (57); HRMS m/z (M^+) calcd for $C_9H_{14}O_3$ 170.0943, found 170.0947.

To a solution of **11** (220.0 mg, 1.29 mmol) in THF (2.0 mL) was added via syringe 5% oxalic acid (2 mL) and stirred for 2 h, after which the solution was added with saturated $NaHCO_3$ to adjust the pH to 6–7. The mixture was extracted sequentially with ether and ethyl acetate several times. After solvent workup, a colorless liquid of **6b**[28] (144.4 mg, 89%) was obtained.

5.8. 4-(*tert*-Butyldimethylsiloxy)-2-cyclohexenone (6c)

To a solution of **6a** (127.0 mg, 1.13 mmol) in benzene (2.3 mL) were added TBDMSCl (1.0 M in THF; 1.25 mL) and DBU (189.7 mg, 1.25 mmol); the resulting mixture was stirred for 2 h. To the reaction mixture were added ether (10 mL) and water (5 mL) and then shaken for several minutes. After discarding the aqueous layer, the ether layer was washed with 0.10 M HCl (5.0 mL×2) and neutralized with $NaHCO_3$. The organic layer was finally washed with saturated NaCl, dried (Na_2SO_4), filtered, and concentrated under vacuo; the crude extract was purified by flush column (hexanes/ethyl acetate, 20:1) to afford a colorless liquid **6c** (229.6 mg, 90%). IR (neat): 2945, 2858, 1687, 1468, 1382, 1253, 1100, 957, 853, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.78 (ddd, J=9.8, 1.9, 1.9 Hz, 1H), 5.87 (dd, J=9.8, 1.3 Hz, 1H), 4.47 (m, 1H), 2.51 (ddd, J=17.2, 4.5, 4.5 Hz, 1H), 2.29 (ddd, J=17.2, 12.8, 4.5 Hz, 1H), 2.18–2.13 (m, 1H), 2.00–1.93 (m, 1H), 0.86 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 153.7, 128.6, 66.9, 25.7, 18.0, −4.7, −4.9; MS (EI, 75 eV) m/z (rel intensity) 227 (M^++1, 3), 211 (8), 198 (3), 169 (100), 151 (47), 127 (7), 125 (6), 95 (9), 75 (62), 73 (18); HRMS (EI) calcd for $C_{12}H_{22}O_2Si$ 226.1389, found 226.1398.

5.9. General procedures for photorearrangement

Unless stated otherwise, photoreactants were placed in Pyrex tubes and dissolved in an appropriate solvent. The resulting mixture was degassed by bubbling argon gas (1 h) and then irradiated with 350 nm light until the reaction was complete. Solvents were removed under reduced pressure and purification of crude products was done by column chromatography using ethyl acetate/hexanes as eluant.

*5.9.1. Irradiation of **4** in benzene (1.0 M).* A solution of **4** (325 mg, 2.11 mmol) in benzene (1.0 M) was irradiated for 48 h. After solvent workup, the residue was separated in a silica gel column (ethyl acetate/hexanes, 1:1) to afford **4** (94 mg) and mixture of **12a**,**b** (180 mg, 78% yield). Recrystallization of the mixture from EtOH/$CHCl_3$ (1:4) afforded a white crystalline solid **12a** (mp 207–209 °C). Workup of the supernatant liquid and recrystallization from DCM/EtOH furnished a white powder, **12b** (mp 222–224 °C).

*5.9.1.1. cis-anti-cis-6,9-Bis(ethylenedioxy)tricyclo[6.4.0.0^{2,7}]dodecan-3,12-dione (**12a**).* IR (KBr): 1702, 1480, 1336, 1272, 1023, 984, 886, 722; ^1H NMR (400 MHz, $CDCl_3$): δ 3.91–3.98 (m, 8H), 3.23 (apparent d, J=7.1 Hz, 2H), 3.00 (apparent d, J=7.1 Hz, 2H), 2.46–2.64 (m, 4H), 2.00∼2.14 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 210.2, 106.8, 65.1, 64.5, 45.5, 43.1, 37.1, 31.1; MS (EI, 75 eV) m/z (rel intensity) 308 (M^+, 13), 265 (14), 251 (11), 209 (5), 179(4), 155 (13), 125 (4), 99 (100); HRMS (EI) calcd for $C_{16}H_{20}O_6$ (M^+) 308.1259, found 308.1255. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33%; H, 6.54%. Found: C, 62.27%; H, 6.57%.

*5.9.1.2. cis-anti-cis-3,9-Bis(ethylenedioxy)tricyclo[6.4.0.0^{2,7}]dodecan-6,12-dione (**12b**).* IR (KBr): 1705, 1287, 1218, 1119, 1063, 1020, 944 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.92–4.04 (m, 8H), 3.08 (m, 4H), 2.57 (m, 4H), 1.97–2.27 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2, 106.7, 65.2, 64.6, 44.2, 44.1, 37.0, 30.3; MS (EI, 75 eV) m/z (rel intensity) 308 (M^+, 30), 265 (22), 251 (12), 209 (4), 181 (4), 155 (25), 125 (4), 99 (100); HRMS (EI) calcd for $C_{16}H_{20}O_6$ (M^+) 308.1259, found 308.1264. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33%; H, 6.54%. Found: C, 62.06%; H, 6.52%.

*5.9.1.3. Ratio determination of dimers **12a** and **12b** in different solvent systems.* Using the procedure above, compound **4** was subjected to photochemical reactions in different solvents: ethylacetate, *tert*-butanol, ethanol, 2,2,2-trifluoroethanol, methanol, and acetonitrile. The relative composition of dimers was determined by gas chromatography; 5 uL of the mixed dimers (1.0 M in ethylacetate) was injected into the GC column (OV-17 1/8″×4 m) equipped with an FID detector. The temperature of the column was set at 120–270 °C and ramped at 10 °C/min; gas flowrate at 18 mL/min. The ratio of **12a** (retention time=28.5 min) and **12b** (retention time=25.7 min) was determined based on the peak area of the two dimers (see Table 1).

*5.9.2. Irradiation of **4** in benzene (0.010 M).* A solution of **4** (321 mg, 2.08 mmol) in benzene (0.010 M) was irradiated for 50 h. The reaction mixture was stripped off of solvent and the residue was separated in a silica gel column (dichloromethane/ethyl acetate/hexanes, 1:1:2) to afford **4** (105 mg) and a white solid, **13** (57 mg, 18%) (mp 123–124 °C), which can be recrystallized from ethanol.

*5.9.2.1. cis-anti-cis-9-Ethylenedioxytricyclo[6.4.0.0^{2,7}]dodec-3,5-en-12-one (**13**).* IR (KBr): 2926, 1712, 1653, 1559, 1175, 1036, 947, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.56–6.62 (m, 2H), 6.13∼6.19 (m, 2H), 3.86–4.07 (m, 4H), 3.77 (apparent t, 1H), 3.58 (apparent t, 1H), 2.23∼2.28 (m, 3H), 1.92 (t, J=6.9 Hz, 2H), 1.59 (d, J=12.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 210.5, 140.0, 138.6, 130.4, 130.2, 110.4, 65.1, 64.9, 52.5, 50.1, 36.6 (CH), 36.6 (CH_2), 35.2 (CH), 35.2 (CH_2); MS (EI, 75 eV) m/z (rel intensity) 232 (M^+, 8), 175 (11), 160 (6), 146 (46), 131 (9), 126 (27), 99 (69), 87 (100); HRMS (EI) calcd for $C_{14}H_{16}O_3$:232.1099, found:232.1099. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39%; H, 6.94%. Found: C, 72.34%; H, 6.98%.

*5.9.3. Irradiation of **4** in tert-butanol (0.010 M).* Following the procedure for **13**, monoketal **4** (323 mg, 2.10 mmol) in *tert*-butanol (0.010 M) was subjected to the same photochemical conditions and the photoproducts were separated on silica gel column (ethyl

acetate/hexanes, 1:1) to obtain **4** (146 mg), **14** (41 mg, 23%), and dimers **12a**,**b** (36 mg, 20%).

*5.9.3.1. 2′-Hydroxyethyl-3-oxocyclopentanecarboxylate (**14**).* IR (KBr): 3415, 2945, 1728, 1398, 1198, 1080, 1028, 894 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ 3.59 (br s, 2H), 2.87 (br s, 1H), 2.73 (m, 1H), 2.45 (dd, J=18.1, 7.7 Hz, 1H), 2.15 (dd, J=18.1, 7.7 Hz, 1H), 2.06∼2.11 (m, 1H), 1.75∼1.87 (m, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ: 215.0, 174.4, 66.4, 60.8, 40.9, 40.8, 37.0, 26.5; MS (EI, 75 eV) m/z (rel intensity) 172 (M^+, 10), 144 (31), 128 (6), 111 (48), 100 (96), 84 (100), 72 (7), 55 (96); HRMS (EI) Calcd for $C_8H_{12}O_4$:172.0736, Found:172.0725.

*5.9.4. Irradiation of **4** in 2,2,2-trifluoroethanol (0.010 M).* Under similar photochemical conditions, irradiation of **4** (312 mg, 2.03 mmol) in TFE (0.010 M) and separation of photoproduct in a silica gel column (ethyl acetate/hexane, 2:1) afforded **14** (273 mg, 78%) as the sole product.

*5.9.4.1. Ethyl-3-oxocyclopentanecarboxylate (**15**).* A solution of **14** (240 mg, 1.39 mmol) and K_2CO_3 (20 mg, 0.14 mmol) in ethanol (14 mL) was stirred at 42 °C for 3 h, after which the solution was quenched with HCl (0.30 M) and extracted with ethyl acetate several times; the organic layer was collected, washed with saturated NaCl, dried ($MgSO_4$), concentrated under reduced pressure, and chromatographed in silica gel column (ethyl acetate/hexanes, 2:3) to afford a colorless oil **15** (173 mg, 79%). IR (KBr): 2974, 1737, 1462, 1405, 1375, 1199, 1158, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.05 (q, J=7.2 Hz, 2H), 3.03 (quintet, J=7.9 Hz, 1H), 1.98∼2.42 (m, 6H), 1.16 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 216.4, 174.0, 60.7, 40.9, 40.7, 37.1, 26.3, 13.9; MS (EI, 75 eV) m/z (rel intensity) 156 (M^+, 13), 128 (66), 111 (27), 100 (58), 83 (67), 73 (9), 55 (100), 45 (5).

*5.9.5. Irradiation of **5a**.* Vinyl ketone **5a** (170.1 mg, 0.93 mmol) in TFE (93 mL) was irradiated for 16 h to furnish a colorless liquid **16** (142.7 mg, 90%) and recover a small amount of **5a** (10.8 mg, 6%). IR (neat) 2964, 1727, 1453, 1328, 1223, 1128, 1076, 1032, 924 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 3.06 (s, 3H), 3.09–3.00 (m, 1H), 2.96 (s, 3H), 2.78 (apparent q, J=5.6 Hz, 1H), 2.68–2.65 (m, 1H), 2.60 (dd, J=8.2, 3.0 Hz, 2H), 2.55–2.50 (m, 1H), 2.26 (ddd, J=11.1, 7.2, 5.2 Hz, 1H), 1.60 (d, J=11.1 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 208.9, 102.9, 49.9, 49.6, 49.5, 47.6, 38.4, 36.3, 32.7, 27.1; MS (EI, 75 eV) m/z (rel intensity) 182 (M^+, 3), 154 (34), 139 (19), 128 (8), 123 (40), 107 (13), 101 (100), 88 (46), 79 (35), 75 (3); HRMS m/z (M^+) calcd for $C_{10}H_{14}O_3$ 182.0942, found 182.0945.

*5.9.6. Irradiation of **5b**.* Dimethyldimethoxy cyclohexenone **5b** (45.1 mg, 0.25 mmol) in TFE (25 mL) was irradiated for 1.6 h. After solvent workup, the residue was purified in a column (hexanes/ethyl acetate, 8:1) to furnish a white solid **17**[13] (16.9 mg, 45%).

*5.9.7. Irradiation of **5c**.* Butyldimethoxy cyclohexenone **5c** (123.4 mg, 0.158 mmol) in TFE (58 mL) was irradiated for 27 h. After removing the solvent in a rotavap, the residue was purified in a column (hexanes/ethyl acetate, 15:1) to afford a colorless liquid **18** (51.1 mg, 26%).

*5.9.7.1. 5-n-Butyl-4-methoxy-4-(2′,2′,2′-trifluoroethoxy)-2-cyclohexenone (**18**).* IR (neat) 2943, 1691, 1462, 1417, 1383, 1281, 1165, 1124, 1071, 968 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 6.00 (dd, J=10.4, 2.0 Hz, 1H), 5.90 (dd, J=10.4, 0.8 Hz, 1H), 3.57–3.48 (m, 1H), 3.37–3.28 (m, 1H), 2.95 (s, 3H), 2.75 (ddd, J=17.2, 4.6, 1.6 Hz, 1H), 2.49 (ddd, J=17.2, 3.2, 1.2 Hz, 1H), 2.06–2.03 (m, 1H), 1.45–1.40 (m, 1 H) 1.32–0.92 (m, 5H), 0.86 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 197.3, 144.2, 132.8, 125.4, 100.8, 61.0, 48.5, 41.5, 39.5, 30.2, 28.8, 23.6, 14.7; MS (EI, 75 eV) m/z (rel intensity) 280 (M^+, 0.2), 238 (14), 223 (2), 196 (100), 181 (21), 167 (13), 121 (8), 113 (50), 93 (7), 55 (10); HRMS m/z (M^+) calcd for $C_{13}H_{19}O_3F_3$ 280.1286, found 280.1284.

*5.9.8. Irradiation of **5d**.* Dimethoxycyclohexenone **5d** (33.8 mg, 0.11 mmol) in TFE (11.3 mL) was irradiated for 1.3 h. After solvent workup, the residue was purified in a column (hexanes/ethyl acetate, 10:1) to afford a yellowish liquid **19** (11 mg, 27%).

*5.9.8.1. 4-Methoxy-4-(2′,2′,2′-trifluoroethoxy)-2-(tert-butyldimethylsiloxymethyl)-2-cyclohexenone (**19**).* IR (neat) 2938, 1685, 1463, 1277, 1148, 1067, 1008, 972, 928, 846, 779 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 6.98 (m, 1H), 4.60 (dd, J=3.2, 2.0 Hz, 2H), 3.60 (qd, J=8.8, 0.8 Hz, 2H), 3.06 (s, 3H), 2.43–2.39 (m, 2H), 1.76–1.71 (m, 1H), 1.66 −1.61 (m, 1H), 1.02 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 196.0, 140.4, 138.2, 122.8, 97.8, 59.5, 58.9, 48.5, 34.3, 31.3, 25.6, 25.5, 25.4, 18.0, −6.0; MS (EI) m/z (%) 368 (M^+, 1), 337 (9), 311 (69), 279 (12), 249 (22), 211 (12), 197 (15), 181 (20), 169 (31), 155(7), 137 (7), 109 (8), 73 (27), 57 (100); HRMS m/z (M^+) calcd for $C_{15}H_{27}O_4F_3Si$ 368.1631, found 368.1634.

*5.9.9. Irradiation of **6a**.* A solution of **6a** (110.4 mg, 0.99 mmol) in TFE (100 mL) was irradiated for 40 h. After solvent workup, the crude photoproduct was separated in a silica gel column (hexanes/ethyl acetate, 2:1) to afford a colorless liquid **20**[28] (87.9 mg, 80%).

*5.9.10. Irradiation of **6b**.* Cyclohexenone **6b** (105.5 mg, 0.84 mmol) in TFE (84 mL) was irradiated for 52 h to furnish a colorless liquid **21**[14] (74.6 mg, 80%) and recover a small amount of **6b** (15.0 mg, 14%).

*5.9.11. Irradiation of **6c**.* Cyclohexenone **6c** (109.8 mg, 0.49 mmol) in trifluoroethanol (49 mL) was irradiated for 32 h to afford a colorless liquid stereoisomers **22a**,**b** (79.4 mg, 53%).

*5.9.11.1. 3-[{[1-(tert-Butyl)-1,1-dimethylsily]oxy}(2,2,2-trifluoroethoxy)methyl]-1-cyclopentanones (**22a**).* IR (neat) 2946, 2860, 1745, 1405, 1278, 1162, 1071, 1002, 839, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.87 (d, J=4.7 Hz, 1H), 3.92–3.72 (m, 2H), 2.46–2.42 (m, 1H) 2.38–2.30 (m, 1H), 2.24 (d, J=8.1 Hz, 2H), 2.18–2.03 (m, 2H), 1.85–1.79 (m, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.4, 124.0, 100.2, 63.0, 42.2, 39.0, 37.6, 25.6, 24.3, 18.0, −4.5, −4.6; MS (EI) m/z (%) 325 (M^+−1, 0.4), 269 (43), 243 (13), 227 (15), 169 (36) 157 (7), 115 (16), 113 (25), 95 (15), 77 (100), 67 (58), 57 (31); HRMS m/z (M^+) calcd for $C_{14}H_{25}O_3F_3Si$ 326.1526, found 326.1530.

*5.9.11.2. 3-[{[1-(tert-Butyl)-1,1-dimethylsily]oxy}(2,2,2-trifluoroethoxy)methyl]-1-cyclopentanones (**22b**).* IR (neat) 2946, 2860, 1745, 1468, 1407, 1276, 1071, 1158, 1002, 841, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (d, J=4.9 Hz, 1H), 3.92–3.75 (m, 2H), 2.46–2.43 (m, 1H), 2.31–2.25 (m, 2H), 2.16–2.03 (m, 3H), 1.95–1.88 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.3, 124.0, 100.1, 63.0, 42.1, 40.2, 37.7, 25.5, 23.2, 17.9, −4.6, −4.7; MS (EI) m/z (%) 325 (M^+−1, 3), 309 (51), 269(100), 249 (8), 227 (13) 193 (6), 171 (7), 127 (6), 113 (21), 95 (12), 67 (51), 55 (19); HRMS m/z (M^+) calcd for $C_{14}H_{25}O_3F_3Si$ 326.1526, found 326.1530.

*5.9.12. Transformation of **22a**,**b** to **20**.* To a solution of **22a**,**b** (32.2 mg, 0.10 mmol) in MeCN (0.8 mL) was added 48% HF (0.2 mL) at room temperature. The reaction mixture was stirred for 1 h and then quenched with water (1 mL). The solution was extracted with $CHCl_3$ (3.0 mL×3) and the organic layer collected, worked up, and

subjected to column chromatography (hexanes/ethyl acetate, 2:1) to obtain a colorless liquid **20** (8.8 mg, 80%).

Acknowledgements

We gratefully acknowledge the financial support from the National Science Council (NSC) of Taiwan.

Supplementary data

^{1}H NMR of **5a**–**d**, **6a**–**c**, **8**–**11**, **12a**,**b**, **13**–**16**, **18**–**21**, **22a**,**b**; ^{13}C NMR of **12a**,**b**, **13**–**15**; 2D-NOESY of **13**; ^{1}H 2D-COSY of **13**; ^{13}C–^{1}H 2D-COSY of **13**; ^{13}C–^{1}H COSY of **16**. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.09.037.

References and notes

1. (a) Eaton, P. E. *Acc. Chem. Res.* **1968**, *1*, 50; (b) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135; (c) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453; (d) Becker, D.; Haddad, N. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, NY, 1989; p 1; (e) Liao, C.-C. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Soon, P.-S., Eds.; CRC: New York, NY, 1995; p 194; (f) Fleming, S. A.; Bradford, C. L.; Gao, J. J. In *Organic Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker: New York, NY, 1997; p 187; (g) Kobayashi, S.; Jorgensen, K. A. *Cycloaddition Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2002; (h) Hoffman, N. *Chem. Rev.* **2008**, *108*, 1052; (i) Hehn, P.; Müller, C.; Bach, T. In *Handbook of Synthetic Photochemistry*; Albini, A., Fagnoni, M., Eds.; Wiley-VCH: Weinheim, Germany, 2010; p 171.
2. (a) Corey, E. J.; Bass, J. D.; Le Mahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570; (b) de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41; (c) Schuster, D. I.; Lem, G.; Kaprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3; (d) Rudolph, A.; Weedon, A. C. *Can. J. Chem.* **1990**, *68*, 1590.
3. (a) Zimmerman, H. E.; Wilson, J. W. *J. Am. Chem. Soc.* **1964**, *86*, 4036; (b) Zimmerman, H. E.; Lewis, R. G.; McCullough, J. J.; Padwa, A.; Staley, S. W.; Semmelhack, M. *J. Am. Chem. Soc.* **1966**, *88*, 1965; (c) Zimmerman, H. E.; Rieke, R. D.; Scheffer, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 2033; (d) Zimmerman, H. E.; Hancock, K. G. *J. Am. Chem. Soc.* **1968**, *90*, 3749; (e) Zimmerman, H. E.; Lewin, N. *J. Am. Chem. Soc.* **1969**, *91*, 879; (f) Zimmerman, H. E.; Solomon, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 6276; (g) Chapman, O. L. In *Advances in Photochemistry*; Noyes, W. A., Jr., Hammond, G. S., Pitts, J. N., Eds.; Interscience: New York, NY, 1963; p 323.
4. (a) Chapman, O. L.; Weiss, D. S. *Org. Photochem.* **1973**, *3*, 197; (b) Schuster, D. I. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, NY, 1980; Vol. 3, p 167; (c) Margaretha, P. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W. M., Ed.; CRC: Boca Raton, FL, 2004; pp 76–81.
5. Dauben, W. G.; Shaffer, G. W.; Vietmeyer, N. D. *J. Org. Chem.* **1968**, *33*, 4060.
6. Chapman, O. L.; Rettig, T. A.; Griswold, A. A.; Dutton, A. I.; Fitton, P. *Tetrahedron Lett.* **1963**, *4*, 2049.
7. Lai, A.-K.; Liao, C.-C. *J. Chin. Chem. Soc.* **1992**, *39*, 423.
8. (a) Hung, S.-C.; Liao, C.-C. *J. Chin. Chem. Soc.* **1994**, *41*, 191; (b) Yu, J.-Q.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, *125*, 3232; (c) Lu, Y.; Nguyen, P. L.; Lévaray, N.; Lebel, H. *J. Org. Chem.* **2013**, *78*, 776.
9. Stern, A. J.; Rohde, J. J.; Swenton, J. S. *J. Org. Chem.* **1989**, *54*, 4413.
10. Doty, B. J.; Morrow, G. W. *Tetrahedron Lett.* **1990**, *31*, 6125.
11. Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
12. Noyce, D. S.; Fessenden, J. S. *J. Org. Chem.* **1959**, *24*, 715.
13. (a) Smith, L. I.; Tess, R. W. H. *J. Am. Chem. Soc.* **1944**, *66*, 1523; (b) Syper, L. *Synthesis* **1989**, *3*, 167.
14. (a) Soderberg, B. C.; York, D. C.; Hoye, T. R.; Rehberg, G. M.; Suriano, J. A. *Organometallics* **1994**, *13*, 4501; (b) Monte, W. T.; Baizer, M. M.; Little, R. D. *J. Org. Chem.* **1983**, *48*, 803.
15. Yates, P.; Ege, S. N.; Buchi, G.; Knutsen, D. *Can. J. Chem.* **1967**, *45*, 2927.
16. (a) Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351; (b) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486.
17. (a) Challand, B. D.; de Mayo, P. *J. Chem. Soc., Chem. Commun.* **1968**, 982; (b) Berenjian, N.; de Mayo, P.; Sturgeon, M. E.; Sydnes, L. K.; Weedon, A. C. *Can. J. Chem.* **1982**, *60*, 425.
18. (a) Schenck, G. O. *Chem. Ber.* **1965**, *98*, 3854; (b) Suppan, P. *J. Photochem. Photobiol., A: Chem.* **1990**, *50*, 293; (c) Singh, A. K.; Bhasikuttan, A. C.; Palit, D. K.; Mittal, J. P. *J. Phys. Chem. A* **2000**, *104*, 7002; (d) Ley, C.; Morlet-Savary, F.; Jacques, P.; Fouassier, J. P. *Chem. Phys.* **2000**, *255*, 335.
19. Bauslaugh, P. G. *Synthesis* **1970**, 287.
20. Loutfy, R. O.; de Mayo, P. *J. Am. Chem. Soc.* **1977**, *99*, 3559.
21. Chapman, O. L. In *Advances in Photochemistry*; Noyes, W. A., Jr., Hammond, G. S., Pitts, J. N., Eds.; Interscience: New York, NY, 1963; p 323.
22. (a) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486; (b) Zimmerman, H. E.; Crumrine, D. S.; Dopp, D.; Huyffer, P. S. *J. Am. Chem. Soc.* **1969**, *91*, 434; (c) Fleming, M.; Basta, R.; Fisher, P. V.; Mitchell, S.; West, F. G. *J. Org. Chem.* **1999**, *64*, 1626.
23. (a) Berson, J. A.; Davis, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 3658; (b) Gleiter, R.; Gubernator, K. *J. Org. Chem.* **1981**, *46*, 1247; (c) Yang, N. C.; Noh, T.; Gan, H.; Halfon, S.; Hrnjez, B. J. *J. Am. Chem. Soc.* **1988**, *110*, 5919; (d) Noh, T.; Yang, N. C. *J. Am. Chem. Soc.* **1991**, *113*, 9412.
24. (a) Saltiel, J.; Charlton, J. L. In *Rearrangement in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, NY, 1980; Vol. 3, p 25; (b) Turro, N. J. *Modern Molecular Photochemistry*; University Science Books: Sausalito, CA, USA, 1991.
25. (a) Buchi, G.; Goldman, I. M. *J. Am. Chem. Soc.* **1957**, *79*, 4741; (b) Srinivasan, R.; Carlough, K. H. *J. Am. Chem. Soc.* **1967**, *89*, 4932; (c) Agosta, W. C.; Wolff, S. *J. Org. Chem.* **1980**, *49*, 3139; (d) Clemens, M. T. M.; McMurry, T. B. H. *J.Chem. Soc., Chem. Commun.* **1986**, 1104.
26. Hammond, M. L.; Zambias, R. A.; Chang, M. N.; Jensen, N. P.; Mcdonald, J.; Thompson, K.; Boulton, D. A.; Kopka, I. E.; Hand, K. M.; Opas, E. E.; Luell, S.; Bach, T.; Davies, P.; MacIntyre, D. E.; Bonney, R. J.; Humes, J. L. *J. Med. Chem.* **1990**, *33*, 908–918.
27. Ochoa, M. E.; Arias, M. S.; Aguilar, R.; Delgado, F.; Tamariz, J. *Tetrahedron* **1999**, *55*, 14535.
28. Colombo, L.; Gennari, C.; Resnati, G.; Scolastico, C. *Synthesis* **1981**, *3*, 74.